

# THE LABORATORY DIAGNOSIS OF POLIOMYELITIS.

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THE Meningitis Division of the Department of Health was established six years ago in order to afford to the physicians of the city of New York expert assistance in the diagnosis and treatment of meningitis. Since 1910 we have held consultations in nearly 1,600 cases, presenting a great variety of meningeal conditions. These have included tuberculous meningitis, purulent meningitis of all kinds (meningococcic, pneumococcic, streptococcic, influenzal, staphylococcic); meningism in a variety of diseases, especially pneumonia, gastro-enteritis and other acute infections in children; many rarer conditions, such as brain abscess, brain tumor, syringomyelia, etc.; and over 500 cases of poliomyelitis, alone, 70 of which occurred before the incidence of the recent epidemic. During the epidemic, doubtful cases have been reported to us for diagnosis. As our work in the past had consisted in a careful clinical study of the cases, combined with various laboratory procedures, especially the examination of the spinal fluid, which we withdrew if the conditions seemed to warrant it, we had had experience that was particularly valuable to us in diagnosing these doubtful cases, for there is no purely "laboratory diagnosis" of poliomyelitis during the life of the patient though the laboratory aid in doubtful

cases is indispensable. The development of experimental poliomyelitis in a monkey inoculated with an emulsion of the brain and cord of a patient who has died of the disease, makes the diagnosis. But if a monkey develops poliomyelitis after being inoculated with the washings of the nose and throat of a case, without the history and clinical findings, one cannot be sure that it is not a carrier rather than a true case. Moreover, on account of the varying susceptibility of monkeys and the small amount of virus present in the nose and throat washings, such a large number of negative results are obtained that the method would be unsuitable for routine diagnosis, even if it were not so expensive and did not take so long for results to develop.

These objections apply also to the neutralization test. This test consists in incubating a mixture of blood serum from a suspected case with a known active virus. This mixture is inoculated intracerebrally in one monkey and the virus alone in a control. The presence of antibodies in the serum is demonstrated if the control monkey becomes infected while the other monkey does not. A further objection to this method lies in the fact that the serum of many people known not to have had a recent attack of poliomyelitis shows the presence of antibodies. Other blood examinations

are of little or no value. The count shows, as a rule, a leucocytosis and a polynucleosis, which is true of most infections with which poliomyelitis may be confounded. The complement fixation has so far been unsuccessful.

The examination of the urine has no diagnostic importance so far as is known at present. At first, it shows the characteristics of an acute febrile condition, later in the paralyzed cases, the end reaction of the products of muscle degeneration. Clinically, it should be noted that in the severe cases there is often a retention of urine, in the very severe cases occasionally a suppression.

The examination of the spinal fluid is the most valuable laboratory aid in the diagnosis of poliomyelitis, but even here, there are no pathognomonic findings, as for example, the infecting organism in a purulent or a tuberculous meningitis. It is by ruling out other conditions that it is of value and it is of the greatest service only when correlated with a careful clinical study of the case. (Of course no diagnosis is easier clinically than that of poliomyelitis with a frank flaccid paralysis, but few diagnoses are more difficult, clinically, than the non-paralytic and atypical cases, which are so important from the standpoint of epidemiology.)

During the recent epidemic, we have examined over 1,800 fluids from both the paralyzed and non-paralyzed cases, nearly 500 of these being from cases which we had seen in their homes.

The data from this material has not yet been entirely arranged as certain facts relating to our own cases have

not been collected and there is yet considerable work to be done in studying the cytology of smears from the centrifuged fluids. Not wishing to give incomplete data nor to burden you with unnecessary details, I will give the more general facts and conclusions from the data that I have studied.

The spinal fluid in poliomyelitis is usually increased in amount and escapes under pressure. It is clear or slightly hazy in appearance and sometimes shows the febrin web formation which was formerly considered pathognomonic of tuberculous meningitis. Recently, attention has been called to the "ground glass" appearance (or a slight haziness seen in the fluid when viewed by strong transmitted light) as being of help in diagnosing poliomyelitis fluid. This appearance is found in the fluids containing the larger number of cells. When the cells are fewer, I, personally, should hesitate to say from the macroscopic appearance whether or not the cells are increased. Moreover, this appearance is also seen in the fluids of tuberculous meningitis, in early purulent meningitides with a slight cellular reaction and in normal fluids where there is a small amount of blood present. In view of these facts, the "ground glass" appearance is of little more significance than the increased quantity. If a bedside examination of the fluid is necessary, one should go with the proper equipment to make a fairly reliable examination.

In poliomyelitis, the spinal fluid shows evidence of an inflammatory reaction—there is a varying increase in

the cells and in the albumin and globulin. In a few cases these evidences of an inflammatory reaction are well marked; in most cases they are moderate; while in a few cases, at the other extreme, they are so slight and the fluid so nearly approaches normal that it is difficult to make a definite statement in regard to the findings. The reduction of Fehling's in these fluids is practically always as prompt as in normal fluids.

The technic which we employ in examining spinal fluids is as follows:

All clear or slightly cloudy fluids are centrifuged for an hour at high speed. From the sediment, spreads are made, taking care to use as nearly as possible, the same area on the different slides. The sediments of clear fluids are stained by the Ziehl-Nielsen method for the tubercle bacillus—the sediments of slightly cloudy fluids for both the tubercle bacillus and by the Gram method. Smears from the poliomyelitis fluids were also made for special blood stains in order to study the cells. This work has not been completed. From this stained sediment, we can estimate the increase in cells as slight, moderate, great, or very great. We do not feel that the exact number of cells has more than an academic interest. The cell count in poliomyelitis and tuberculous meningitis, while on the average higher in the latter, overlaps for so wide a range as to render the differential diagnosis by this point most unreliable. Moreover, while some claims to the contrary have been made, it is not our impression that the number of cells in poliomyelitis fluids bear

any relation to the prognosis of the case. We have made a fair number of cell counts in connection with the work and we find that, on the whole, the two methods check up fairly well. From these stained sediments we also estimate the percentage of mononuclears and polymorphonuclears and note the presence of endothelioid and polyform cells. The presence or absence of bacteria is also noted. Cultures are made from all specimens. In the case of uncontaminated poliomyelitis fluids, they have been uniformly negative.

The chemical tests that we use are the nitric acid ring test for albumin and the Noguchi butyric acid test for globulin. The albumin and globulin practically always run parallel, but they serve as a check on each other. The small amount of albumin and globulin present in normal fluids is marked  $\pm$ . The signs, +, +!, ++, + + +, + + + +, represent increasing amounts and serve as a rough quantitative estimation. The presence of glucose is tested by using an equal amount of Fehling's solution and spinal fluid and it is marked with regard to the speed and the amount of reduction as -,  $\pm$ , +, ++, + + +. The globulin reaction and the reduction of Fehling's should not be read for at least half an hour.

Taking up these points somewhat in detail, let us first consider the cytology. The increase in cells varies very greatly both in different cases and in the stage at which the puncture is done. Our counts have varied from slightly above normal, 15–20 to 350–400. The counts tend to fall off after the first week and

by the end of the second week have fallen to practically normal in nearly all cases.

The cells usually show a preponderance of mononuclears but in a few instances there is over 50 per cent. of polymorphonuclears. It has been stated that early in the disease there was an excess of polymorphonuclears, which later was replaced by mononuclears. In the large number of early fluids that we have examined on the second, third, and fourth days, the polymorphonuclears—out of a special series of about 400 fluids in only 3 cases, occurring on the third, fourth, and fifth days respectively. We feel, therefore, that the polymorphonuclears represent a special type of reaction—and is not characteristic of a stage of the disease. Often, even in fresh fluids, the cells are so degenerated that it is difficult to classify them. There are large mononuclear cells that seem to be endothelial in type that seem to us to occur more frequently in poliomyelitis than in other conditions. The so-called polyform cells are also found. We hope to study the various types of cells more carefully a little later.

The albumin and globulin are usually slightly to moderately increased. In 141 fluids, 99 were marked + or + 1; 36, ++ or +++ 1; 5, +++; and 1, ++++. The increase in albumin and globulin persists after the cell count has returned to normal.

Fehling's, as has been stated before, is practically always well reduced. The fluids that show a poorer reduction are usually those with the larger amount of albumin and globulin.

We will now consider the differential diagnosis of poliomyelitis fluids.

The slightly cloudy fluids must be differentiated from those of early cases of purulent meningitis and from the slightly cloudy fluid that occasionally occurs in tuberculous meningitis. The clear or practically clear fluids, from rare early cases of a purulent meningitis, tuberculous meningitis, syphilis of the central nervous system, especially acute syphilitic meningitis, and meningism. Other rarer conditions might be mentioned, but these are the most important.

In early cases of purulent meningitis, the spinal fluid shows a varying degree of cloudiness, except in very rare instances, when it may be clear. A greater increase in albumin and globulin is usually found here than occurs in poliomyelitis, with a poorer reduction of Fehling's solution. The cells in these fluids of purulent meningitis are 90 per cent. or more polymorphonuclears, and the etiological organism is always found except in the mildest cases. In certain mild cases of meningitis—probably of the epidemic variety—the meningococci may never be positively demonstrated in the fluid. In purulent meningitis, due to other organisms, these practically always appear later. In one instance only, we have seen a clear fluid from an early case of epidemic meningitis of about eighteen hours' standing. Although the cellular reaction was so slight, the meningococcus was demonstrated to be present in the fluid by smear and culture.

The fluid in tuberculous meningitis most nearly resembles that of polio-

myelitis. It is practically always clear with a cellular increase consisting largely of mononuclears, though in very acute cases it may be distinctly cloudy with an excess of polymorphonuclears. Fortunately, in these cases, the tubercle bacillus is usually easy to demonstrate. The number of cells per cubic millimeter is usually greater than in poliomyelitis; the increase in albumin and globulin is more marked, and the reduction of Fehling's is not so good.

In rare instances when clinical signs are confusing and when the results of the cellular examination and chemical analysis are indefinite, and it is impossible to demonstrate the tubercle bacillus in the fluid, a positive diagnosis must wait upon the results of animal inoculation.

The fluid of an acute syphilitic meningitis closely resembles the fluid of a poliomyelitis, and the clinical signs are also confusing. The Wassermann reaction is the best method of differentiating the two conditions.

Of course, a positive Wassermann would not rule out a poliomyelitis in an old syphilitic condition, but this, combined with the clinical condition and the progress of the case, makes one reasonably sure of the diagnosis. It was suggested at first that the products of degeneration present in the spinal fluid of poliomyelitis cases might give a non-specific Wassermann reaction. Repeated tests have proved this not true.

The fluid of meningism is clear, increased in amount and practically always normal in character. The few exceptions to this that we have

found in a large series of cases have fallen mainly into three groups: fluids from cases with prolonged and severe convulsions; fluids in severe whooping-cough; and fluids removed just prior to death. In these cases there have sometimes occurred an increase in cells, or in albumin and globulin or in both. In convulsions, there is probably oedema, in whooping-cough minute hemorrhages, and just before death circulatory changes to account for it.

Lange's colloidal gold test has been used to some extent by workers to whom we have given specimens of fluid and it would seem that it may be helpful in differentiating the fluids of poliomyelitis from those of tuberculous meningitis and from the fluids of meningism which are not normal in character.

Two rare types of spinal fluids sometimes occur in poliomyelitis when the hemorrhagic process has been more than usually severe. The first of these is of the true hemorrhagic character, the red blood cells being evenly diffused throughout the field. When collected in successive tubes the specimens are all homogenous, showing no change in the intensity of the hemorrhage. This serves to differentiate it from bloody fluids obtained by the accidental puncture of a vein.

Evidence of an older hemorrhage occurs in the second of these rarer fluids, which, having a characteristic yellow color and coagulating spontaneously, illustrates the so-called syndrome of Froin. These fluids occur in other conditions, and are, therefore, not pathognomonic of poliomyelitis.

During the past four months, we have done some quantitative work on the chemistry of the poliomyelitis fluids using the micro-chemical methods. This work will be published in detail later. In brief, I may state that it has been found that the *total nitrogen* runs 20–30 mgms. per 100 cc.

Of this total nitrogen about one-half is non-protein and about one-fourth is urea.

Creatinin—.5 mgm. in 100 cc. fluid.

Creatin—.3 mgm. in 100 cc. fluid.

Sugar is slightly lower than in the blood—.05 per cent.—.08 per cent.

All show traces of cholesterol.

In conclusion, I wish to state again that there is no specific laboratory diagnosis of poliomyelitis during life though the laboratory findings are of the greatest possible aid; that physicians can most successfully diagnose the doubtful cases who have had the most experience with the clinical study of meningeal conditions of all kinds, correlated with the laboratory study of the spinal fluids.



### THE HEALTH BULLETIN.

The health officer has ever had a variety of duties. What with controlling foci of infection, inspecting suspected food, and offensive privies, protecting water supplies, draining swamps, and determining the fate of sundry noisy and sleep disturbing fowls of a neighborhood, he has had enough to keep him thinking and acting. Recently, however, he has had thrust upon him the business of editor, and often author, of a weekly or monthly publication in the interests of public and private health. Though presumably unprepared for such a service the health officer has risen to the occasion remarkably well.

The issuance of a bulletin was not a new thing for the health department, for a statement of the number of cases of this and that disease and the number of deaths, the number of diagnostic tests made, and a summary of other work, had often been published. But the new bulletin deals with matters of life and health rather than disease and death—in a word, with prophylaxis. The statistics, which we fear were seldom scanned, occupy the background in this new literary venture.

In its present (though we doubt its final) stage of evolution, the health bulletin is often an amphibious affair, intended for both the profession and the public, and for this and other reasons, appealing less than it might, to either. The material intended for physicians is often of a nature perplexing to the laity. In fact we have seen such material so poorly worded or badly edited that the medical reader himself

was sorely puzzled as to its meaning. In other cases members of the health staff, excellent in their special lines of bacteriological or other work, have put things in a way which has thrown doubt upon their efficacy. Careful editing would have prevented such a misfortune.

On the "popular" side the health bulletin has too often accepted the usual notion that in order to appeal to the public, one must highly color, or in other words, a little, if not considerably, exaggerate the facts. If this is the key to the lay mind, the earlier the key is lost the better. But the layman is not so stupid. You can fool him some of the time but not always, and exaggerations always react upon their source.

When it comes to sensational methods in health education the health bulletin cannot hold a candle to the advertisers of curealls, for they not only have the literary cleverness, but they have the financial backing. Their reading matter is not sent "to those who desire it" but is spread broadcast and reaches a hundred homes where the health bulletin reaches one. The competition is most one sided, but truth and dignity will prevail even over lies. The kingdom of health, like that kingdom of heaven of which it is an essential part, is like a grain of mustard seed and will surely grow and increase. Let us avoid doing anything that will delay that growth. The health bulletin is an aid toward furthering the kingdom, but let it be worthy of its cause.—Editorial, *New York Medical Journal*, January 27, 1917.